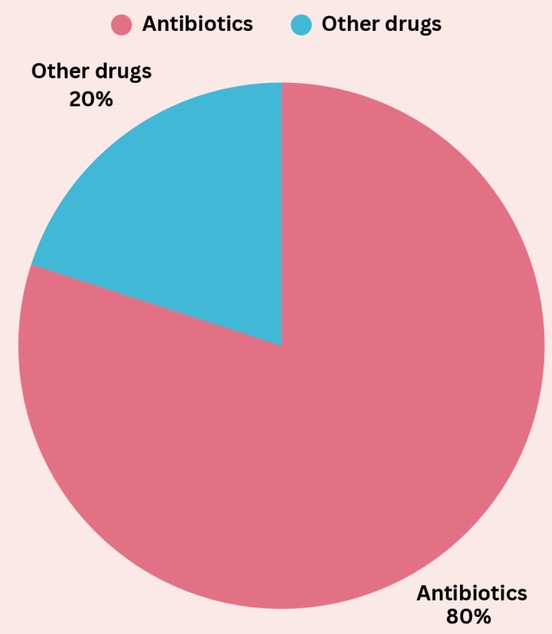
FCPI STAT DOSE

SAFE ANTIBIOTIC USE IN PREGNANCY

Antibiotics make up nearly 80% of all prescriptions during pregnancy.

Around 20–25% of pregnant women will receive an antibiotic at some point during their pregnancy.



Common infections for which the antibiotics are prescribed in pregnancy include:

- Urinary tract, most common
- Genital tract
- Skin and soft tissues
- Respiratory tract

Risks of untreated infections include: Fetal transmission, Low birth weight, Preterm birth.

If the risk of untreated infection is greater than the risk of the drug ↠ prescribe the antibiotic.

TIMING OF EXPOSURE AND RISKS

First trimester:
Greatest risk for major birth defects (organ formation occurs here).

Second and third trimesters: Risks shift to
- Growth problems
- Minor birth defects
- Functional defects (e.g., kidney or liver function issues)
- Learning difficulties in the child.

FDA PREGNANCY AND LACTATION LABELING RULE (PLLR)

Background

Before 2015: Drugs were labeled with letter categories (**A, B, C, D, X**) to indicate pregnancy safety, but these were often confusing.

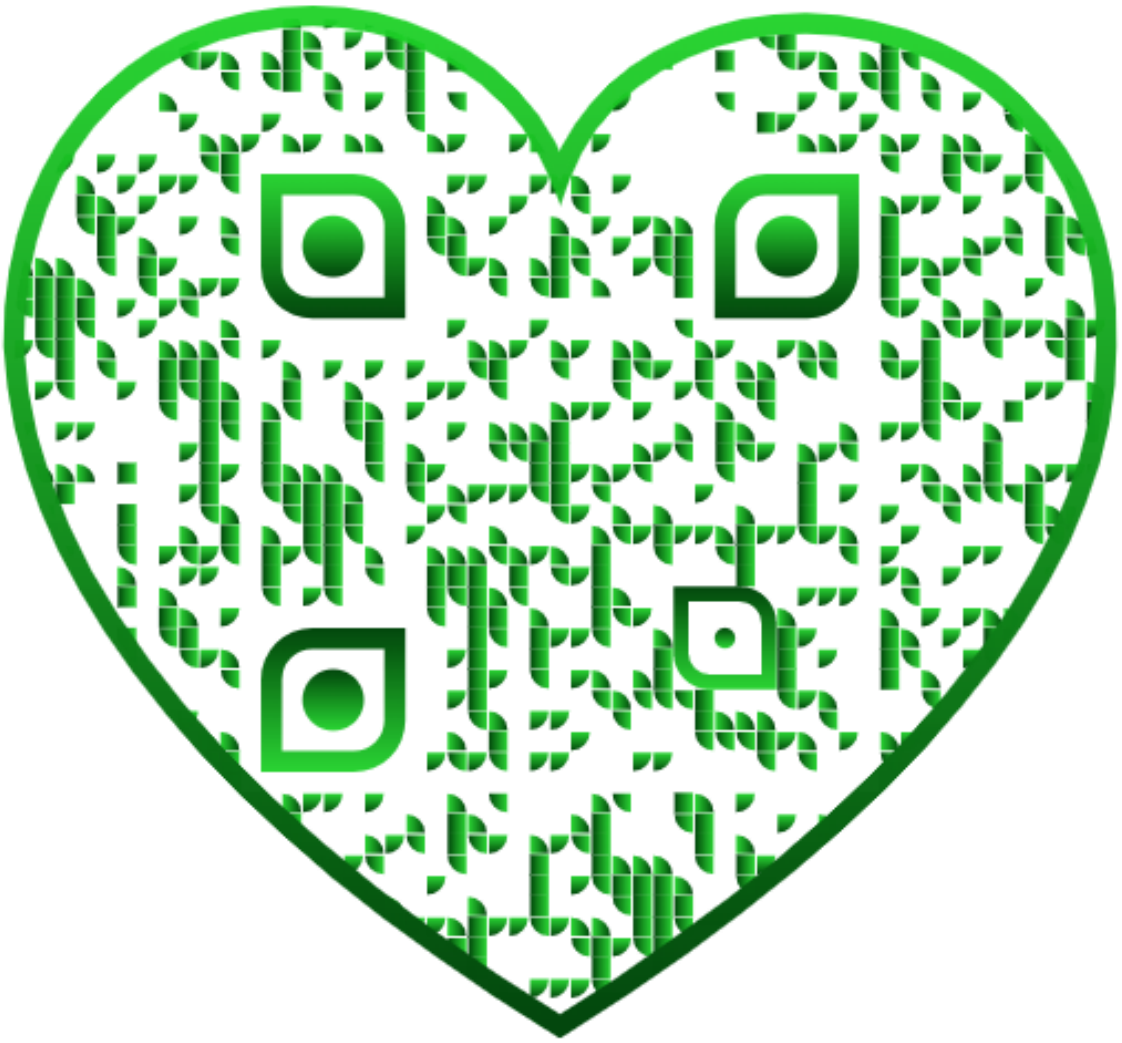
2015: The FDA introduced the **Pregnancy and Lactation Labeling Rule (PLLR)** to provide clearer, narrative information.

KEY FEATURES OF PLLR:

Divides drug labeling into three mandatory sections:

PREGNANCY:	Subsections: Risks, clinical considerations, and data
LACTATION:	Safety of drugs during breastfeeding
♀ & ♂ OF REPRODUCTIV -E POTENTIAL:	Effects on fertility, contraception, and pregnancy testing.

- Cephalosporins and metronidazo are the most prescribed antibioti in pregnancy.
- Early exposure can alter the neonatal gut microbiome, increasing the risk of obesity & IBD.
- Antibiotic resistance may lead to complicated infections like pyelonephritis.



ANTIBIOTIC SAFETY PROFILE IN PREGNANCY: FCPI STAT DOSE

Antibiotic Class	Prior FDA category	Trimester Consideration	Key Risks	Clinical Recommendations	Updated Data
Penicillins	**B**	All trimesters	Minimal fetal risk	First-line for many infections	Well-established safety
Cephalosporins	**B**	All trimesters (avoid ceftriaxone at term)	Kernicterus risk with ceftriaxone at term	Preferred for UTIs and other infections	Ceftolozane/tazobactam, cefiderocol, ceftobiprole: animal data favorable
Carbapenems / Monobactams	**B**	All trimesters	Minimal fetal risk	Use when indicated for serious infections	Established safety; sulopenem: limited data
Clindamycin	**B**	All trimesters	Minimal fetal risk	Use for gram-positive or anaerobic infections	2017 labeling confirms safety
Fosfomycin	**B**	1st trimester	Minimal fetal risk	First-line UTI therapy	2023 French study supports safety
Vancomycin	**B**	2nd/3rd trimester preferred	Nephrotoxicity risk; monitor levels	Use for serious gram-positive infections	Supported by case reports
Metronidazole (Topical)	**B**	All trimesters	Minimal fetal risk	Topical use safe anytime	Well-studied
Nitrofurantoin	**B**	Avoid at term; safe 1st trimester	Hemolytic anemia risk at term; contraindicated in neonates <1 month	First-line UTI except at term	Long-established safety
Beta-lactamase inhibitors (BLIs)	**B**	All trimesters	Minimal fetal risk; limited data for new BLIs	Safe with beta-lactams; monitor if using newer agents	Avibactam: 2023 case report safe; others: limited animal data

Antibiotic Class	Prior FDA category	Trimester Consideration	Key Risks	Clinical Recommendations	Updated Data
Aminoglycosides (Except Topical)	**D**	**Highest risk 1st trimester**	Fetal ototoxicity, vestibular deficits	Avoid streptomycin; short-term use of others only if no alternatives; monitor maternal renal function	Animal/human data; systemic exposure harmful
Daptomycin	**B**	2nd/3rd trimester	Monitor dosing >8–10 mg/kg	Use for resistant infections with monitoring	Multiple case reports support safety
Macrolides (Clarithromycin, Azithromycin)	**Azithro B, Clarithro C**	1st trimester	↑ spontaneous abortion risk; cardiovascular defects	Use only if necessary	Conflicting data (Denmark vs UK studies)
Fidaxomicin	**● (not assigned)**	All trimester	Limited systemic absorption; data limited	Use only if benefits outweigh risks	Low oral bioavailability supports cautious use
Oxazolidinones (Linezolid)	**C**	All trimester	Limited data; MDR tuberculosis	Use for multidrug-resistant infections	New TB data: 27 pregnant patients, no increased risk
Rifabutin / Rifaximin	**C**	All trimesters	Limited data; teratogenicity in animals	Use with monitoring	Limited human data

Antibiotic Class	Prior FDA category	Trimester Consideration	Key Risks	Clinical Recommendations	Updated Data
Rifampin / Rifapentine	**C**	All trimesters	Rifampin: postpartum hemorrhage; monitor coagulation	Use with monitoring; vitamin K if needed	Rifapentine: 50-patient study favorable
Metronidazole (Systemic 1st Trimester)	**B**	Avoid 1st trimester; safe later	70% ↑ spontaneous abortion risk if systemic	Use only 2nd/3rd trimester if needed	Avoid in pregnancy; contraception required
Fluoroquinolones	**C**	All trimesters	Fetal renal toxicity, CNS defects, cardiac malformations	Use only if no alternatives	Established risk
Tetracyclines / Glycylcyclines (Doxycycline, Tigecycline, Eravacycline, Omadacycline)	**D/●**	All trimesters	Teratogenicity, skeletal defects, reduced fetal weight	Only for tick-borne or life-threatening infections	Established risk; new agents expected similar
Lefamulin	**●**	All trimesters	Animal data: fetal harm	Avoid in pregnancy; contraception required	Animal studies only
Polymyxin B / E	**●**	All trimesters	Nephrotoxicity, neurotoxicity	Use as last-line therapy	Limited human data
Pretomanid	**●**	All trimesters	No human data; WHO recommends against use	Avoid in pregnancy	New anti-TB agent
Sulfamethoxazole/Trimethoprim	**D (1st tri), C (later)**	Avoid 1st trimester unless essential	Folic acid antagonism; congenital risk	Supplement with 4 mg folic acid if 1st trimester use required	Use only when first-line therapy necessary

Antibiotic Class	Prior FDA category	Trimester Consideration	Key Risks	Clinical Recommendations	Updated Data
Telavancin	●	All trimesters	Boxed warning: fetal risk	Avoid in pregnancy	Limited data

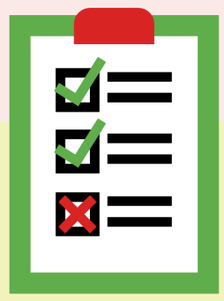
🟢 Safe; 🟡 Caution; 🔴 Avoid

CLINICAL PRACTICE GUIDELINES

Antimicrobial Stewardship in Pregnancy

Key Principles:

- Bacterial eradication often imperative for maternal and fetal safety
- Shortest effective duration to minimize fetal exposure
- Preference for agents with established safety profiles
- Avoidance of first trimester exposure when clinically feasible



Risk-Benefit Assessment Framework

Essential Components:

1. Multidisciplinary approach involving obstetrics, pharmacy, and infectious disease specialists
2. Thorough risk assessment considering maternal infection severity vs. fetal risks
3. Patient counseling regarding potential risks and benefits
4. Monitoring protocols for both maternal and fetal well-being

Special Considerations

- **Antibiotic Resistance:** Increasingly observed in pregnant women with active infections and linked to complicated cases such as pyelonephritis.
- **Timing of Therapy:** Whenever possible, avoid antibiotic exposure during the first trimester; opt for safer alternatives in the second and third trimesters.
- **Monitoring Needs:** Certain agents require close maternal and fetal surveillance (e.g., rifamycins for bleeding risk, aminoglycosides for potential ototoxicity and nephrotoxicity).

Post-Marketing Surveillance (Critical Need): Continued pharmacovigilance for newly approved agents without pregnancy data, particularly: **Ceftobiprole, Enmetazobactam, Durlobactam/Sulbactam, Sulopenem, Etzadroxil/Probenecid.**

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Nguyen J, Madonia V, Bland CM, Stover KR, Eiland LS, Keating J, Lemmon M, Bookstaver PB, as part of the Southeastern Research Group Endeavor (SERGE-45) research network. "A review of antibiotic safety in pregnancy—2025 update." Pharmacotherapy. 2025;45(4):227–237. doi:10.1002/phar.70010.